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TITLE: Initial Randomized Controlled Trial Acceptance and Commitment Therapy (ACT) for Distress and Impairment in OEF/OIF Veterans

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14. ABSTRACT

During the past 12 months, this study has received approval from the WRAMC Dept. of Clinical Investigation IRB. All necessary staff and personnel have been hired and have completed all required training. Study enrollment is underway and early data collection has begun. These milestones correspond to the goals set by the study timeline and indicate that progress is occurring on schedule despite unexpected delays regarding the BRAC process at Walter Reed. At this time there are no significant findings to report.

15. SUBJECT TERMS
PTSD, TBI, ACT, cognitive-behavioral therapy, military populations

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Introduction

Combat leads to "psychological injury," including posttraumatic stress disorder (PTSD) and other anxiety disorders and depression, in at least a substantial minority of combatants (Hoge et al., 2004). In addition, many combatants in Iraq and Afghanistan are exposed to blasts or blows to the head that may lead to head injury, which can be followed by postconcussive symptoms (PCS; McAllister & Arciniegas, 2002). There is a strong need for treatment of the complex array of problems that follow combat, specifically for non-pharmacologic treatments as these are preferred by many veterans and military personnel. Current approaches are not effective and/or acceptable for all affected individuals, so finding new ways to deal with the sequelae of deployment is important. Acceptance and Commitment Therapy (ACT) is a psychotherapeutic approach that holds promise for this group. ACT is not tied to any particular symptom constellation, so it can be applied to a variety of presenting concerns. It has good face validity and conveys a compelling message, asking individuals to move forward in accordance with one's values regardless of limitations, and ACT offers an alternative for people who refuse exposure-based approaches. Because of the enthusiasm for the approach, ACT is being widely disseminated – but without evidence for its effectiveness for military trauma. There is evidence of its effectiveness for emotional distress in general (Forman et al., 2007) and for depression in particular (Zettle & Hayes, 1986; Zettle & Rains, 1989) but not in military samples or for deployment-related distress.

The primary objective of this multi-site randomized controlled trial is to determine if receiving ACT, as compared to a control psychotherapy, is associated with reduced distress at the end of treatment. We will also examine its impact on functioning and acceptability as well as the extent to which gains are maintained after treatment. We will gather preliminary information about the impact of ACT on symptoms specific to PTSD, depression and PCS to inform future studies. In addition, we will gather information about the acceptability of and response to ACT in active duty service people as compared to those receiving care from the VA. Although the project is separately funded and administered, it is being conducted within the structure of the DoD-funded PTSD/TBI Clinical Consortium (INTRuST Consortium).

The primary objective of this trial is to evaluate the efficacy of ACT for reducing symptoms in veterans of Operation Enduring Freedom and/or Operation Iraqi Freedom and/or Operation New Dawn (OEF/OIF/OND).

Objective 1: To determine if receiving ACT, as compared to PCT, is associated with reduced distress as measured by the BSI-18 General Symptom Index (GSI) at the end of treatment. There are three secondary objectives of the trial. First, we are interested in determining whether or not the impact of ACT extends beyond reduced general distress to anger, a common problematic associated symptom, and functioning. Second, we have hypothesized that an advantage of ACT is its acceptability. Thus, we will evaluate how participants receive it. Finally, we are interested in the degree to which gains are maintained after treatment. Early maintenance

of treatment effects (3 months) will be assessed in the entire sample. Longer-term follow-up will be completed for the patients who enroll earlier to provide preliminary data about longer-term outcomes.

Objective 2: To determine if receiving ACT, as compared to PCT, is associated with reduced anger and functional impairment at the end of treatment.
Objective 3: To compare the acceptability of ACT and PCT for OEF/OIF/OND veterans.
Objective 4: To describe to what extent treatment gains are sustained after treatment with ACT.

This project also has exploratory objectives. We chose to include patients with a variety of deployment-related presenting complaints because we believe that this is more representative of the way in which ACT would be applied in practice and because we believe that the broad applicability of the intervention is a strength of the approach. Nonetheless, it will ultimately be useful to understand whether or not there are groups for whom ACT is more or less helpful. Although we cannot recruit enough participants in this trial to have adequately powered disorder-specific comparisons, we plan to collect preliminary data that can direct future research on this topic. Similarly, we believe that it is important to inform future work in which ACT may be applied to active duty military personnel.

Objective 5: To assess whether or not ACT as compared to PCT is associated with decreased disorder-specific symptoms in subgroups with PTSD, Major Depression and post-concussive symptoms.

Objective 6: To gather preliminary information regarding the acceptability of and response to ACT in active duty service people as compared to those receiving care from the VA.

Objective 7: To compare the impact of the interventions on posttraumatic growth, hope, guilt and insomnia and to evaluate potential mediators of change.

Body

The overall study is a randomized controlled trial of Acceptance and Commitment Therapy (ACT). However, WRAMC subjects will participate only in one arm of the study, a pilot study in which all service members will receive ACT therapy and there will be no control group or need for randomization. The following is an overview of the approved study design that is currently being implanted across all study sites:

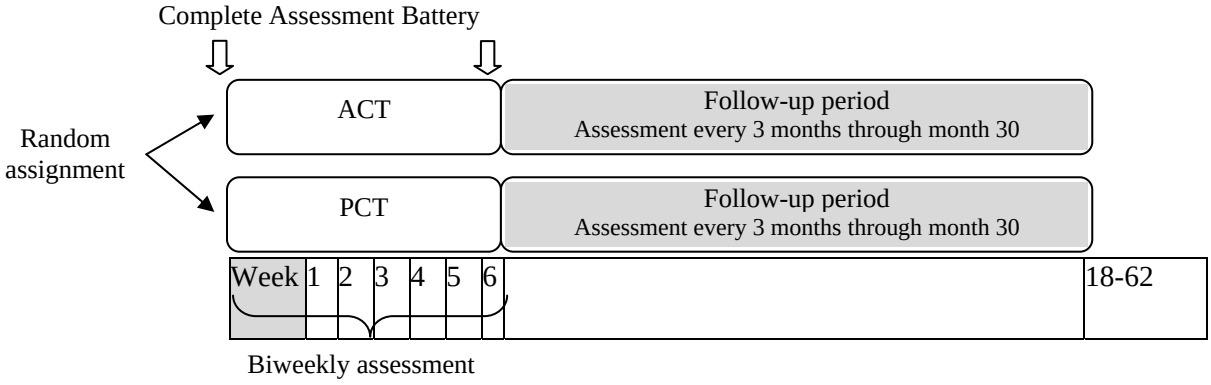

Figure 1: Study Timeline

Screening Visit: Informed Consent and Eligibility Assessment

- Review of study, obtain Informed Consent, sign HIPAA Authorization.
- Semi-structured clinical interview and neuropsychological screening by study assessor to determine eligibility.
- Participant completes self-administered questionnaires. Active duty respondents at Walter Reed are not eligible to receive the $25 dollar incentive that civilian study participants will receive at the other study locations.

Visits 1-12 Treatment Sessions

- Participant completes full assessment battery before session 1 (except credibility, which is given at the end of session 1) and after session 12. Participant receives twelve 60-minute one-on-one treatment sessions of ACT over 6-10 weeks (ideally 2 sessions per week but additional weeks are permissible if needed).
- Periodic brief assessment before sessions 3,5,9 and 11.
- Follow-up treatment sessions and assessments will be scheduled by the therapist with the subjects at the conclusion of each session in accordance with the treatment and assessment schedule. If a subject fails to return for scheduled follow-up, three attempts will be made to contact the subject by phone in accordance with the attached telephone script before the subject is considered to have been withdrawn from the study.

Post- treatment Follow-Up

- Participant completes self-administered questionnaires (via mail or by telephone) every 3 months for up to 12 months after the last session attended. See appendix L for script and cover letter.

At this time, the WRAMC site has enrolled 3 participants this study and all are still undergoing treatment sessions. No participants have yet completed the full course of treatment or begun follow-up sessions at the WRAMC site. Recruitment is ongoing, although there was an anticipated delay while the outpatient behavioral health clinic was transferred from its current site at Walter Reed Army Medical Center to its new home at the Walter Reed National Military Medical Center. This transition resulted in a temporary hold on recruitment as new patients were not being referred to the behavioral outpatient clinic during this period. Across all sites, currently we have 27 participants who have enrolled in the study and 5 participants have completed the study. Data is being sent to the lead site at UC San Diego, however analysis has not yet begun.

Key Research Accomplishments

The following graph displays the approved study timeline for this project. Goals for year 1 of this three year study are detailed below along with a description of how these goals were met.

MILESTONES	2010	2011	2012
Regulatory Review/IRB Approval			
Preparatory & Administrative Tasks			
Informatics			
Hire & Train Study Personnel			
Patient Recruitment & Enrollment			
Follow-up Data Collection & Patient Closeout			
Data Analysis			
Report Writing & Dissemination			

Preparatory Phase (Months 1 – 6)

- Regulatory Review and IRB Approval (Months 1-6): Prepare and submit humans subjects protection application to Site IRBs, VA Research and Development Committees, and Army's Second Tier Office of Research Protections.

  -- Approval from INTRuST Clinical Consortium Coordinating Center was given February 2010. Preparation of human subjects protection at Walter Reed Army Medical Center (WRAMC) began at this time. Project was initially submitted to WRAMC Dept. of Clinical Investigation in July 2010 for IRB approval. Approval process continued through April 2011 to account for ongoing amendments and changes to study protocols made at the lead study site at UC San Diego.

- Hire and Train Study Personnel (Months 3-6)**:** (1) Hire study staff; (2) establish weekly meetings for study execution; (3) train therapists in ACT during week-long training in Palo Alto, CA; (4) train assessors

  -- A study therapist and a clinical assessor were hired in September 2010. Therapist completed ACT training in November 2010. Clinical assessor already had all necessary certifications at time of hire. Regular teleconference meetings have been established and are still ongoing.

- Miscellaneous Preparatory Tasks (Months 1-6)**:** (1) Purchase necessary supplies and transport to study sites; (2) develop study manual of operation and randomization procedures; (3) establish study-specific charter for Consortium DSMB; (5) develop and test standardized audio recording procedures for independent evaluators; and (6) make logistic arrangements with clerical and ancillary staff at participating clinical sites to ensure timely scheduling, intake, and provision of care to study patients.

  -- All necessary supplies have been acquired and study space at WRAMC was established in October 2010. Logistical arrangements with behavioral outpatient clinical staff were carried out at this time to ensure an orderly system for recruitment and monitoring of continued patient care. Master manual of procedures and all study protocols finalized by lead site in August 2010. These protocols and procedures were adapted locally and approved by WRAMC DCI in April 2011.

Patient Recruitment & Enrollment Phase (Months 7 – 24): (1) Identify and recruit potential participants ($n \cong 40$ total per VA clinic, $N = 158$; $n \cong 20$ total at Walter Reed); (2) monitor enrollment progress at clinics; (3) provide ongoing adherence checks and supervision for therapists (Drs. Walser & Bolton); (4) collect data from study participants in accordance with analysis plan; (5) collect and report adverse events and serious adverse events; (6) conduct regular data monitoring for quality assurance; (7) ongoing analyses as requested by DSMB.

-- Recruitment began in April 2011 with the first participant enrolling at WRAMC in May 2011. Recruitment presentations were given at key department meetings to increase rate of patient referrals in May 2011. At time of reporting, there are 3 participants enrolled locally at WRAMC and 27 participants enrolled across all study sites. Study therapist continues to hold regular performance meetings with lead study therapists. Data collection is ongoing, although the proposed Electronic Data Capture system (EDC) was not established on schedule due to delays during software development. Instead, data is copied and sent at monthly intervals back to lead site for eventual analysis. Data monitoring for quality assurance is ongoing with the first external audit due in Q1or Q2 2012.

BRAC Process Transition (Months 7-10): Walter Reed is scheduled for closure on September 15th, 2011. At this time, all hospital facilities and personnel, including any ongoing clinical studies, will be transferred to the Walter Reed National Military Medical Center (WRNMMC). Study personnel at WRAMC will be responsible for: 1) Securing regulatory approval to transition all study operations to WRNMMC; 2) make logistical arrangements for continued recruitment, enrollment and quality of care for all study participants; 3) transfer all necessary study supplies and securely transport any data records; 4) once transition is completed, assess whether any new protocol changes are needed.

-- The behavioral outpatient clinic was moved to WRNMMC in August 2011. The transition statement carrying over IRB approval from WRAMC to WRNMMC was acknowledged by WRAMC DCI in August 2011. The clinical staff was moved over a two week period and new referrals to the clinic were put on hold, effectively putting study recruitment on hold as well. All study files and data records were transferred to the new study space at WRNMMC during this period. New recruitment presentations will be given in September 2011 to remind all clinical staff and targeted general care providers of the study's continued recruitment effort and to provide information on our new location. Ongoing recruitment and enrollment has been somewhat hindered by the BRAC process, although not more than was anticipated.

Reportable Outcomes

Although data collection has only just begun and recruitment has been slowed in the last four months due to the time, attention, and energy of potential referral sources being devoted to processes associated with the transition of care from WRAMC to WRNMMC, participant recruitment, enrollment, and data collection has resumed at the new medical treatment facility at this time.

Presentation related to this study:

Benedek, DM "Fostering Resilience in Returning Combat Veterans," New Jersey Veterans Affairs 8th Annual Best Outcomes, Best Practices Conference, Somerset, NJ, June 2011. (note this presentation did not include data from this trial but this trial was described as part of overview of ongoing clinical intervention trials related to post-deployment distress and PTSD).

Conclusions

This multi-year, multi-site study is designed to determine the efficacy of Acceptance and Commitment Therapy (ACT) in the treatment of distress and impairment related to combat exposure. Such a therapy would prove useful to both VA clinics and active-duty health care providers due to its low cost, ease of training and implementation, and broad range of application. To date, this is the only study that has looked at the efficacy of this therapeutic model in a military population. The eventual results of this study will be greatly instrumental in determining whether such a therapeutic model can be effectively implemented in a military

setting or on other populations that experience similar types of distress and impairment (i.e. emergency first responders, disaster relief workers, etc). Such an outcome could have a significant impact on the availability and quality of mental health treatment and care available to the growing number of combat veterans.

At this time, data collection is only just beginning and has not yet been initiated at all study sites. WRAMC has begun enrollment and data collection, but this data has not yet been analyzed. The primary goal moving forward into Year 2 of the study timeline is to continue recruitment and enrollment until our site participant goal of approx. 20 participants has been achieved. Ongoing efforts to disseminate information about the study at relevant conferences and professional meetings will be increased as data collection continues.

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